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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,279	12/11/2001	Johnny Paul Speir	140-067a	2332

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EXAMINER
KENEDY, ANDREW A

ART UNIT	PAPER NUMBER
1631	

Ward & Olivo
708 Third Ave
New York, NY 10017

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/014,279	SPEIR, JOHNNY PAUL	
	Examiner	Art Unit	
	Andrew A. Kenedy	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-29 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-29 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment of Claims 1, 3, 4, 6, 9, 11, 12 and 14, and addition of new Claims 15-29 in the reply of May 4, 2004, is acknowledged. Claims 1-29 are currently pending.

Response to Arguments

Applicant's arguments with respect to original Claims 1-14 have been considered but are moot in view of the new grounds of rejection presented below. Newly added Claims 15-29 are also rejected under the new grounds of rejection.

The new grounds of rejection were necessitated by Applicants' amendment because of the newly introduced limitations of drug-dosed biological samples, and the identification of metabolites and cellular changes in biological samples resulting from the effects of a drug injected into the samples.

In the response of May 4, 2004, Applicants argue that their invention offers the advantage of being able to immediately analyze chemical changes in complex biological samples. Specifically, Applicants argue that their method enables analysis of all changes in small and large molecules in cellular samples within minutes after drug-dosing the samples, rather than weeks or months after drug-dosing, because it is unnecessary to prepare purified samples of the individual molecules as with previous methods. This argument is moot in light of the newly applied reference, Dasseux et al. (US 2002/0019023 A1), which teaches methods for analysis of both low and high molecular weight (small and large) molecules in complex biological samples, including drug-treated cell samples that are analyzed by FTMS simply and directly with

"minimal preparation such as extraction of the cells or cell lysate into a solvent suitable for FTMS" (see at least the abstract; and pg. 11 [0107]).

The following rejections and/or objections are either reiterated or newly applied, and constitute the complete set presently being applied to Claims 1-29. The text of those sections of Title 35 U.S.C. not included in this action can be found in the previous Office Action.

Claim Rejections - 35 USC § 112

Claims 15, 18, 21, 24 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New Claims 15, 18, 21, 24 and 27 require that "said a drug is injected into said biological sample to create said drug-dosed sample". The instant specification does not disclose injecting a drug into a biological sample. While the specification does disclose injecting a drug into "species" and "test cells", these are not inherently the same as a biological sample. Biological samples are typically subsets derived from animal species and cells. Therefore the above limitation constitutes **new matter** that was not previously disclosed as part of the methods currently claimed.

Claim Rejections - 35 USC § 103

Claims 1-11 and 15-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yates (*Journal of Mass Spectrometry*, January 1998, Vol. 33, pp. 1-19), in view of Dasseux et al. (US 2002/0019023 A1).

Yates is applied as in the previous Office Action mailed October 30, 2003. As explained in the previous action, Yates teaches ionizing biological samples for analysis by FTMS.

However, Yates does not teach a drug-dosed biological sample as in newly amended Claims 1, 4, 6 and 9; injecting drugs to create a drug-dosed biological sample as in newly added Claims 15, 18, 21 and 24; detecting metabolic products as in newly added Claims 16, 19, 22 and 25; or identifying cellular changes of drug-dosed samples as in Claims 17, 20, 23, and 26. Yates also does not teach the limitations of Claims 3 and 11, which were rejected in the previous Office Action over Yates in view of Moore et al. (US 5577239).

Dasseux et al. teaches analyzing biological samples using FTMS, wherein prior to analysis by FTMS, either cell lysates (biological samples) or intact cells are treated with drugs (drug-dosed) (see at least the abstract; pg. 10 [0091]; pg. 5 [0045]; pg. 6 [0053]; and pg. 7 [0062]).

Regarding Claims 3 and 11, Dasseux et al. is now applied in lieu of Moore et al. Dasseux et al. teaches that databases can be generated and updated with information determined using FTMS, including highly accurate molecule databases which can be used in identifying species of molecules present in the sample by comparison to the database (see at least pg. 5 [0047]). Dasseux et al. further teaches that the primary information provided by FTMS is a molecule's

identity and empirical formula, obtained by determining the characteristic stoichiometric sum of the molecular masses of each element in the molecule through FTMS (see pg. 1 [0002]-[0003]).

Regarding Claims 15, 18, 21 and 24, Dasseux et al. uses the term 'added' rather than 'injected' when referring to the method of delivery of the drug to the biological sample. However, Applicants do not disclose or attach any particular meaning to the term "injected" that would indicate any particular mode of delivery or addition. The term 'inject' is routinely used in the art to indicate the addition of drugs or samples to measuring devices, other samples, and living organisms by means of pipets, syringes, and pipets that resemble syringes. For example, Dasseux et al. uses the term "injected" and "injection" when referring to the manual delivery of biological samples into the FTMS instrument itself (see at least pg. 14 [0135]-[0137]). Dasseux et al. also uses the term "injection" to refer to the delivery of drugs into rats, from which hepatocytes (liver cells) were then isolated for further drug treatment with lovastatin followed by analysis using FTMS (see pg. 24 [0247]-[0249]). Dasseux et al. also uses the term "injection" to refer to the delivery of drugs into rats from which blood samples were taken for direct analysis by FTMS in order to characterize drug metabolites (see pg. 26 [0269]-[0270]). Therefore, Applicants use of the term "injected" in the above claims is interpreted to mean the addition of the drug to any sample using routine means in the art such as a pipet or syringe, which is made obvious by the teachings of Dasseux et al. as explained above.

Regarding Claims 16, 19, 22 and 25, Dasseux et al. teaches the detection of metabolic products in the samples (see at least pg. 5 [0046]).

Regarding Claims 17, 20, 23, and 26, Dasseux et al. teaches identifying cellular changes as a result of drug exposure (drug-dosing) in biological samples (see at least pg. 5 [0045]).

It would have been obvious to one of ordinary skill in the art to combine the teachings of Dasseux et al. with the teachings of Yates, since both Dasseux et al. and Yates teach the use of FTMS for analyzing biological samples. Furthermore, Dasseux et al. teaches that FTMS is ideal for analyzing complex biological mixtures such as cells containing both high and low molecular weight molecules (see at least the abstract; and pg. 4 [0040]), and that a distinct advantage of the invention is the ability to discover/screen new drug candidates by exposing cells to drugs and then analyzing the resulting sample by FTMS (see at least pg. 4 [0043] – pg. 5 [0045]).

Claims 12-14 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yates (*Journal of Mass Spectrometry*, January 1998, Vol. 33, pp. 1-19) and Franzen et al. (US 5663561), in view of Dasseux et al. (US 2002/0019023 A1).

Yates and Franzen et al. are applied as in the previous Office Action mailed October 30, 2003.

Yates and Franzen et al. do not teach a drug-dosed biological sample as in newly amended Claim 12; injecting drugs to create a drug-dosed biological sample as in newly added Claim 27; detecting metabolic products as in newly added Claim 28; or identifying cellular changes of drug-dosed samples as in Claim 29. Yates also does not teach the limitations of Claim 14, which was rejected in the previous Office Action over Yates in view of Moore et al. (US 5577239).

Dasseux et al. teaches analyzing biological samples using FTMS, wherein prior to analysis by FTMS, either cell lysates (biological samples) or intact cells are treated with drugs

(drug-dosed) (see at least the abstract; pg. 10 [0091]; pg. 5 [0045]; pg. 6 [0053]; and pg. 7 [0062]).

Regarding Claim 14, Dasseux et al. is now applied in lieu of Moore et al. Dasseux et al. teaches that databases can be generated and updated with information determined using FTMS, including highly accurate molecule databases which can be used in identifying species of molecules present in the sample by comparison to the database (see at least pg. 5 [0047]). Dasseux et al. further teaches that the primary information provided by FTMS is a molecule's identity and empirical formula, obtained by determining the characteristic stoichiometric sum of the molecular masses of each element in the molecule through FTMS (see pg. 1 [0002]-[0003]).

Regarding Claim 27, Dasseux et al. uses the term 'added' rather than 'injected' when referring to the method of delivery of the drug to the biological sample. However, Applicants do not disclose or attach any particular meaning to the term "injected" that would indicate any particular mode of delivery or addition. The term 'inject' is routinely used in the art to indicate the delivery of both drugs and samples to measuring devices, other samples, and living organisms using pipets, syringes, and pipets that resemble syringes. For example, Dasseux et al. uses the term "injected" and "injection" when referring to the manual delivery of biological samples into the FTMS instrument (see at least pg. 14 [0135]-[0137]). Dasseux et al. also uses the term "injection" to refer to the delivery of drugs into rats from which hepatocytes (liver cells) were then isolated for treatment with the drug lovastatin, followed by analysis using FTMS (see pg. 24 [0247]-[0249]). Dasseux et al. also uses the term "injection" to refer to the delivery of drugs into rats from which blood samples were taken for direct analysis by FTMS in order to characterize drug metabolites (see pg. 26 [0269]-[0270]).

Regarding Claim 28, Dasseux et al. teaches the detection of metabolic products in the samples (see at least pg. 5 [0046]).

Regarding Claim 29, Dasseux et al. teaches identifying cellular changes as a result of drug exposure (drug-dosing) in biological samples (see at least pg. 5 [0045]).

It would have been obvious to one of ordinary skill in the art to combine the teachings of Dasseux et al. with the teachings of Yates and Franzen et al., since both Dasseux et al. and Yates teach the use of FTMS for analyzing biological samples. Furthermore, Dasseux et al. teaches that FTMS is ideal for analyzing complex biological mixtures such as cells containing both high and low molecular weight molecules (see at least the abstract; and pg. 4 [0040]), and that a distinct advantage of the invention is the ability to discover/screen new drug candidates by exposing cells to drugs and then analyzing the resulting sample by FTMS (see at least pg. 4 [0043] – pg. 5 [0045]).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew A. Kenedy whose telephone number is (571)-272-0574. The examiner can normally be reached on Monday-Friday 9:00am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571)-272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A.A.K. June 10, 2004

MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
6.14.04